

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A method for producing a humanized antibody comprising VH and VL variable regions of an animal antibody of known sequence, comprising the steps of:

- a) obtaining a crystallographic structure of the VH and VL regions of the animal antibody;
- b) pre-selecting a series of 0 to n possible framework acceptors of human origin or humanized antibodies, whose structure was determined experimentally with a resolution of no greater than 2.5 Å, wherein selected framework acceptors have the highest level of homology and identity with the primary sequence of the framework of the animal antibody;
- c) conducting a structural comparison between the VH and VL variable regions of the animal antibody and the VH and VL regions of the framework acceptors of human origin, respectively and ~~calculating for each comparison~~ comparing the value of the root mean square deviation (RMS, Å), to identify the VH region and the VL region of human origin with the smaller RMS; wherein the RMS is (RMS) calculated between atoms of alpha carbon constituting the respective amino acid skeletons, not considering atom pairs with an RMS exceeding 2Å, and comparing percentages of atoms on which RMS was calculated, and comparing a similitude index between primary structures to identify the VL region of human origin with the smaller RMS; and
- d) inserting in appropriate position the sequences of a CDR region of the animal antibody into the VH region and the VL region of human origin identified in c).

2. (Previously Presented) The method of claim 1, wherein the modifications of the antibody take place with recombinant DNA techniques.

3-7. (Canceled)

8. (Withdrawn/Previously Presented) A humanized anti-NGF antibody comprising a VH region having the amino acid sequence set forth in SEQ ID NO:17 and a VL region having the amino acid sequence set forth in SEQ ID NO: 18, or a fragment thereof which maintains NGF binding activity.
9. (Withdrawn/Previously Presented) A humanized anti-TrkA antibody comprising a VH region having the amino acid sequence set forth in SEQ ID No. 37, and a VL region having the amino acid sequence set forth in SEQ ID No. 38, or a fragment thereof which maintains TrkA binding activity.
10. (Withdrawn/Previously Presented) An immunotoxin comprising a cytotoxic agent bound to a humanized anti-TrkA antibody comprising a VH region having the amino acid sequence set forth in SEQ ID No. 37, and a VL region having the amino acid sequence set forth in SEQ ID No. 38, or a fragment thereof which maintains TrkA binding activity.
11. (Withdrawn/Previously Presented) A method for treating inflammation in a subject by administering a humanized anti-NGF antibody comprising a VH region having the amino acid sequence set forth in SEQ ID NO:17 and a VL region having the amino acid sequence set forth in SEQ ID NO: 18, or a fragment thereof which maintains NGF binding activity.
12. (Withdrawn/Previously Presented) A method for treating pain in a subject by administering a humanized anti-NGF antibody humanized anti-NGF antibody comprising a VH region having the amino acid sequence set forth in SEQ ID NO:17 and a VL region having the amino acid sequence set forth in SEQ ID NO: 18, or a fragment thereof which maintains NGF binding activity.
13. (Withdrawn/Previously Presented) A method for treating a tumor in a subject by administering a humanized anti-NGF antibody humanized anti-NGF antibody comprising a VH region having the amino acid sequence set forth in SEQ ID NO:17 and a VL region having the

amino acid sequence set forth in SEQ ID NO: 18, or a fragment thereof which maintains NGF binding activity.

14. (Withdrawn/Previously Presented) A method for treating an HIV induced pathology in a subject by administering a humanized anti-NGF antibody comprising a VH region having the amino acid sequence set forth in SEQ ID NO:17 and a VL region having the amino acid sequence set forth in SEQ ID NO: 18, or a fragment thereof which maintains NGF binding activity.

15. (Withdrawn/Previously Presented) A method for treating inflammation in a subject by administering a humanized anti-TrkA antibody comprising a VH region having the amino acid sequence set forth in SEQ ID No. 37, and a VL region having the amino acid sequence set forth in SEQ ID No. 38, or a fragment thereof which maintains TrkA binding activity.

16. (Withdrawn/Previously Presented) A method for treating pain in a subject by administering a humanized anti-TrkA antibody comprising a VH region having the amino acid sequence set forth in SEQ ID No. 37, and a VL region having the amino acid sequence set forth in SEQ ID No. 38, or a fragment thereof which maintains TrkA binding activity.

17. (Withdrawn/Previously Presented) A method for treating a tumor in a subject by administering a humanized anti-TrkA antibody comprising a VH region having the amino acid sequence set forth in SEQ ID No. 37, and a VL region having the amino acid sequence set forth in SEQ ID No. 38, or a fragment thereof which maintains TrkA binding activity.

18. (Withdrawn/Previously Presented) A polynucleotide encoding a humanized anti-NGF antibody comprising a VH region having the amino acid sequence set forth in SEQ ID NO:17 and a VL region having the amino acid sequence set forth in SEQ ID NO: 18, or a fragment thereof which maintains NGF binding activity.

19. (Withdrawn/Previously Presented) A polynucleotide encoding a humanized anti-TrkA

antibody comprising a VH region having the amino acid sequence set forth in SEQ ID No. 37, and a VL region having the amino acid sequence set forth in SEQ ID No. 38, or a fragment thereof which maintains TrkA binding activity.

20. (Withdrawn/Previously Presented) A transgenic animal expressing a humanized anti-NGF antibody comprising a VH region having the amino acid sequence set forth in SEQ ID NO:17 and a VL region having the amino acid sequence set forth in SEQ ID NO: 18, or a fragment thereof which maintains NGF binding activity.

21. (Withdrawn/Previously Presented) A transgenic animal expressing a humanized anti-TrkA antibody comprising a VH region having the amino acid sequence set forth in SEQ ID No. 37, and a VL region having the amino acid sequence set forth in SEQ ID No. 38, or a fragment thereof which maintains TrkA binding activity.

22. (Withdrawn/Previously Presented) A cell expressing a humanized anti-NGF antibody comprising a VH region having the amino acid sequence set forth in SEQ ID NO:17 and a VL region having the amino acid sequence set forth in SEQ ID NO: 18, or a fragment thereof which maintains NGF binding activity.

23. (Withdrawn/Previously Presented) A cell expressing a humanized anti-TrkA antibody comprising a VH region having the amino acid sequence set forth in SEQ ID No. 37, and a VL region having the amino acid sequence set forth in SEQ ID No. 38, or a fragment thereof which maintains TrkA binding activity.

24. (Previously Presented) The method of claim 1, further comprising retromutating one or more amino acid residues of the human VH and VL regions identified in (c).